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In-hospital clinical outcomes after upper gastrointestinal surgery: Data from an international observational study

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Abstract

Aims: Previous research suggests that patients undergoing upper gastrointestinal surgery are at high risk of poor postoperative outcomes. The aim of our study was to describe patient outcomes after elective upper gastrointestinal surgery at a global level.

Methods: Prospective analysis of data collected during an international seven-day cohort study of 474 hospitals in 27 countries. Patients undergoing elective upper gastrointestinal surgery were recruited. Outcome measures were in-hospital complications and mortality at 30-days. Results are presented as n(%) and odds ratios with 95% confidence intervals.

Results: 2139 patients were included, of whom 498 (23.2%) developed one or more postoperative complications, with 30 deaths (1.4%). Patients with complications had longer median hospital stay 11 (6-18) days vs. 5 (2-10) days. Infectious complications were most frequent, affecting 368 (17.2%) patients. 328 (15.3%) patients were admitted to critical care postoperatively, of whom 161 (49.1%) developed a complication with 14 deaths (4.3%). In a multivariable logistic regression model we identified age (OR 1.02 [1.01-1.03]), American Society of Anesthesiologists physical status III (OR 2.12 [1.44-3.16]) and IV (OR 3.23 [1.72-6.09]), surgery for cancer (OR 1.63 [1.27-2.11]), open procedure (OR 1.40 [1.10-1.78]), intermediate surgery (OR 1.75 [1.12-2.81]) and major surgery (OR 2.65 [1.72-4.23]) as independent risk factors for postoperative complications. Patients undergoing major surgery for upper gastrointestinal cancer experienced twice the rate of complications compared to those undergoing other procedures (224/578 patients [38.8%] versus 274/1561 patients [17.6%]).

Conclusions: Complications and death are common after upper gastrointestinal surgery. Patients undergoing major surgery for cancer are at greatest risk.

Introduction

Currently, 310 million patients undergo surgery worldwide each year, with more procedures taking place in high-income countries.[1,2] Estimates of mortality following in-patient surgery vary from 1 to 4%, [3-10] but it is now recognised that selected high-risk patient groups are more likely to develop life threatening complications. Postoperative complications increase treatment costs,[11,12] and reduce both life expectancy and quality of life at a societal level.[3,14] Whilst technical errors are unusual during surgery and anaesthesia, poor patient outcomes persist for a variety of reasons. Improvements in the quality of perioperative care for high-risk patients may therefore lead to better patient outcomes.

Patients undergoing surgery to treat cancer of the upper gastrointestinal tract are an important high-risk group. This includes cancers of the oesophagus, and stomach, which have a poor long-term prognosis. Worldwide, oesophageal cancer is the sixth leading cause of death from cancer.[15] Surgical resection remains the only potentially curative treatment, and is integrated in a multimodal therapy, particularly for advanced disease. Recent data from the United Kingdom suggest one third of patients undergoing oesophageal and gastric surgery for cancer, experience postoperative complications, with hospital mortality rates in the region of 3%.[16] Other reports describe complication rates between 40 and 80%, depending on age, gender, type of surgery, and the presence of chronic disease.[17,18]

The need remains to better understand patient outcomes following upper gastrointestinal surgery, to ensure the planning of effective perioperative care, including appropriate patient selection, surgical approach and postoperative provision of critical care.[14] The International Surgical Outcomes Study (ISOS) was recently conducted to evaluate the incidence and risk factors for complications and death after in-patient elective surgery at a global level, and to describe current standards of postoperative care.[19] ISOS included a prospective sub-group analysis to describe in detail, the clinical outcomes and standards of perioperative care following upper gastrointestinal surgery at a global level, and to describe factors associated with complications during the hospital stay and death in this population.

Patients and Methods

Project organisation

ISOS was approved by the Yorkshire & Humber Research Ethics Committee (Reference: 13/YH/0371). We then conducted a sub-group analysis of data collected during this international seven-day cohort study of outcomes following elective adult in-patient surgery. Regulatory requirements differed between countries with some requiring research ethics approval and some requiring only data governance approval. Each participating country selected a single data collection week between April and August 2014. Patient data included only that recorded as part of routine care. Local investigators were supported by national co-ordinators, the international study management group, and via a website which provided all study documentation and guidance on study procedures (www.isos.org.uk/documents). The main ISOS project was registered prospectively with an international trial registry (ISRCTN51817007). The manuscript has been prepared according to the STROBE statement.[20]

The inclusion criteria were all adult patients (age ≥ 18 years) undergoing elective surgery with a planned overnight stay in hospital. Patients undergoing emergency surgery, day-case surgery or radiological procedures were excluded. We aimed to recruit as many hospitals and countries as possible and asked investigators in those hospitals to enrol all eligible patients. No formal sample size calculation was performed. Only hospitals returning valid data describing ≥ 20 patients and countries with ≥ 10 participating hospitals were included in the primary analysis of the ISOS dataset.[19] In this sub-group analysis, we included all patients who underwent upper gastrointestinal surgery by the thoracic or abdominal route, using either an open or laparoscopic technique, identified via the e-CRF.[19] We also investigated whether there were any differences in outcomes between high-income countries, and low or middle-income countries.

Data collection

Data describing consecutive patients were collected until hospital discharge on paper case record forms. Data were censored at 30 days following surgery for patients who remained in hospital. Data were anonymised before entry onto a secure internet-based electronic case record form designed specifically for ISOS, which incorporated automated checks for plausibility, consistency and completeness.

Outcome measures

The primary outcome measure was in-hospital postoperative complications assessed using predefined criteria and graded according to the Clavien-Dindo classification.[21,22] The secondary outcome measure was in-hospital mortality. Process measures were admission directly to critical care after surgery, admission to critical care for treatment of a postoperative complication, and duration of hospital stay. A single prospective definition of critical care was used for all countries (a facility routinely capable of admitting patients who require invasive ventilation overnight).

Statistical analysis

Statistical analysis was performed using SPSS (version 20.0) and R: A language and environment for statistical computing (R Foundation for Statistical Computing, Vienna, Austria). Categorical variables are presented as number (%) and continuous variables as mean (SD) where normally distributed and median (IQR) where not normally distributed. Univariable analysis was used to select risk factors for postoperative complications. Multivariable logistic regression analysis was used to develop a generic model in which all previously determined risk factors were entered. The threshold for inclusion of variables in the multivariable analysis was $p < 0.05$. All predictors were entered into the model using forced simultaneous entry. With the expected sample size, a limited number of factors could be included in the model without over fitting, and these were selected based on clinical suitability and assessment of correlated variables. Bootstrapping was used to assess the reliability of the models. Goodness-of-fit tests were performed using the Hosmer-Lemeshow test. A process of forward and backward selection, based on minimisation of Akaike's Information Criterion (AIC), was used to derive the final model.[23] Results are presented as odds ratios with 95% confidence intervals. For variables included in our final model, univariable logistic regression was then performed to generate unadjusted odd ratios for comparison with the multivariable model. In the main ISOS database, data describing baseline risk factors were missing for a very small proportion of patients [451/44 814 (1%)]. Due to the low proportion of missing data, we performed a complete case analysis where patients with missing data were excluded from the analysis.[19]

Results

Data describing 44 814 patients were collected in 474 hospitals in the following countries and regions: Australia, Austria, Belgium, Brazil, Canada, China, Denmark, France, Germany, Greece, Hong Kong, Indonesia, Italy, Malaysia, Netherlands, New Zealand, Nigeria, Portugal, Romania, Russia, South Africa, Spain, Sweden, Switzerland, Uganda, United Kingdom, and the United States of America. Fewer than ten hospitals participated in India, Iraq and Mexico and in accordance with the prospective statistical analysis plan, patients recruited in these countries were excluded from the primary analysis. 2139 patients who underwent upper gastro-intestinal surgery in 369 centres were identified in the ISOS database (4 [2-7] patients per centre; Figure 1). Baseline patient data are presented in Table 1.

Process measures

The median stay in a post-anaesthetic care unit was 2 (1-3) hours. 328 (15.3%) patients were admitted to a critical care unit as routine immediately after surgery, with a median critical care stay of 1 (1-4) days. Of these patients, 161 (49.1%) developed a complication with 14 (4.3%) deaths. 121 patients were admitted to a critical care unit to treat complications, of whom 17 (14%) died. The median duration of critical care stay for patients admitted to treat a complication was 5 (1-10) days. The median overall hospital stay was 5 (2-10) days, increasing to 11 (6-18) days amongst those patients who developed complications.

Clinical outcomes

In total, 498 (23.2%) patients developed complications in hospital, and 30 died before hospital discharge (1.4%). 297 (13.9%) patients developed a single postoperative complication whilst 201 (9.4%) patients developed two or more complications. Data describing postoperative complications are presented in Table 2. There were 368 infectious complications affecting 254 patients, the most frequent being pneumonia and superficial surgical site infections of varying severity (Table 2). There were 125 complications affecting 97 patients related to technical aspects of surgery, such as postoperative bleeding and anastomotic leak (Table 2). The “All other” category of complications were not specified and included deep vein thrombosis, ileus, pancreatitis etc. Nine patients experiencing complications in this category died, however, all had additionally experienced infectious, cardiovascular, or other complications related to the technical aspects of the procedure. In the initial univariable regression analysis, age (OR 1.03 [1.02-1.04]), American Society of Anesthesiologists (ASA) physical status score III (OR 3.33 [2.32-4.78]) or IV (OR 5.51 [3.07-9.88]), surgery for cancer (OR 2.60 [2.11-3.21]), non-laparoscopic surgery (OR 1.79 [1.45-2.21]),

intermediate surgery (OR 1.81 [1.19-2.75]), major surgery (OR 4.34 [2.91-6.48]) and cirrhosis (OR 2.28 [1.05-4.95]) were identified as risk factors for postoperative complications. However during the multivariable logistic regression analysis when adjusted for cofounders, only age, ASA status, surgery for cancer, non-laparoscopic surgery, intermediate and major surgery were identified as independent risk factors for postoperative complications (Table 3). This indicated major upper gastrointestinal surgery to treat cancer as a sub-population at particular risk of poor outcomes (Supplementary Table 1), with twice the rate of complications (224/578 major cancer patients [38.8%] versus 274/1561 [17.6%] patients undergoing minor, intermediate, or major non-cancer procedures (Figure 2). In the major cancer surgery group, 122 (21.1%) patients developed one complication, whilst 102 (17.6%) patients developed two or more complications during their postoperative stay in hospital. Of 2139 patients who underwent upper gastrointestinal surgery, 30 died (1.4%). Non-survivors were older, had higher ASA scores and underwent major surgery (Supplementary Table 2).

Comparison of high-income and low or middle-income countries:

Using the World Bank classification, eight were classed as low or middle-income countries (Brazil, China, Indonesia, Malaysia, Nigeria, Romania, South Africa, and Uganda), and 19 were classed as high-income countries (Australia, Austria, Belgium, Canada, Denmark, France, Germany, Greece, Hong Kong, Italy, Netherlands, New Zealand, Portugal, Russia, Spain, Sweden, Switzerland, United Kingdom, and the United States of America).[24] Patient outcomes for major cancer surgery in high-income countries were similar to the overall international sub-group with 326/1270 patients (25.7%) developing complications with six deaths (2.3%). In this post-hoc analysis, complication rates were lower in the low or middle-income countries 172/869 (19.8%) $p < 0.001$. When explored this we found that although age was similar in both the high and low or middle-income countries 57 (44-68) vs 58 (46-66) years, ASA distribution significantly differed with more ASA 2, 3 and 4 patients being operated in the high income countries (Supplementary Figure 1). Patients in high-income countries underwent fewer minor procedures (Supplementary Figure 2). There were no significant differences between high or low and middle-income countries in terms of risk of complications in the univariable analysis.

Discussion

We report data from an international prospective cohort study describing detailed postoperative outcomes for a population of more than 2,000 patients undergoing elective upper gastrointestinal surgery in 27 countries worldwide. The principal findings were that one in four patients experienced a complication before hospital discharge, compared to one in six of the overall surgical population in the parent study.[19] Surgery involving the upper gastrointestinal tract was associated with higher risk of complications compared to the reference category of orthopaedic surgery in the complete ISOS dataset.[19] According to our results, complications in the upper gastrointestinal surgery group were associated with a two-fold increase in hospital stay, and one in fifteen patients who developed a complication died before hospital discharge. Patients undergoing major cancer surgery are at particular risk, with twice the postoperative complication rate of other patients undergoing upper gastrointestinal surgery. In the univariable analysis, risk of complication was similar when high-income countries were compared to low and middle-income countries. Our results suggest that the greater crude complication rates in high-income countries largely relate to differences in casemix. This finding suggests that measures to reduce complication rates remain important in all countries, regardless of income status.

The complication rates observed in this analysis are lower than those reported in recently studies from Sweden, Japan, Australia and the UK.[16,25-27] The Australian, Japanese and UK studies all reported complications during hospital stay, similar to our methods. Unlike our contemporary snapshot of practice, these studies collected information on patients over several years.[25-27] The ongoing change and improvement in clinical practice over the last decade might partly account for the lower observed complication rates in our series.[28] Infectious complications such as surgical site infections and pneumonia remain commonplace, and are associated with prolonged hospital stays. In previous studies, pneumonia rates as high as 22.5% were reported following oesophagectomy, whereas in our series the rate was only 4.0%, even in the major cancer surgery sub-group.[16,25-27] Similarly, technical complications of surgery were less frequent in this dataset, although this may relate to differences in casemix and improvements in surgical technique and perioperative care compared to the standards observed in previous studies in this international patient sample. [16,25-27]

Mortality rates were lower than expected given the observed complication rates. It is possible that this relates to improvements in the care of patients who develop complications, although this may also be affected by the duration of critical care stay for patients who develop life threatening

complications after major elective surgery, which may now routinely exceed 30 days before treatment is withdrawn for reasons of futility. In this context, 30-day mortality may not truly reflect the seriousness of eventual patient outcomes. The risk factors for postoperative complications identified in the ISOS study are well recognised. Age has been shown to be independently associated with higher post-operative morbidity and mortality after major upper gastrointestinal procedures,[29-31] although age alone should not be viewed as a reason to deny patients a definitive surgical treatment. A recent Australian study did not demonstrate any correlation between age and long-term survival, even though postoperative complications were more frequent amongst elderly patients.[31] The findings from our larger international study are consistent with this previous work, confirming the high incidence of complications early after upper gastrointestinal surgery amongst elderly patients. ASA score has been highlighted as a strong predictor of postoperative complications.[32] It is interesting to note that a relatively large proportion of patients undergoing upper gastrointestinal surgery were classed as ASA III or IV, in both cancer and non-cancer cancer groups, with a corresponding increase in the frequency of complications. Similar findings have recently been reported in the UK, with one third of patients undergoing oesophagectomy falling into ASA III and IV categories.[33] Recent recommendations for the treatment of upper gastrointestinal cancer recommend careful patient selection based on physiological reserve and pre-existing co-morbid disease.[34,35] One in six patients in this cohort were admitted to a critical care unit immediately after surgery, half of whom experienced postoperative complications. Although significant progress has been made in the development of perioperative pathways to improve patient outcomes, it remains uncertain what the most appropriate level of postoperative care should be for this high-risk patient group. This is highlighted in the findings of a recent analysis of a large US dataset, which did not identify any benefit of routine critical care admission immediately after major upper gastrointestinal cancer surgery.[36] The secondary analysis of the ISOS dataset also failed to signal any mortality benefit of routine critical care admission following high-risk elective surgery.[37]

The strengths of this study have been discussed in detail in our previous publication.[19] We used a very simple data set consisting primarily of categorical variables to aid data collection and minimising empty data fields. Patient-level variables were selected on the basis that they were objective, and routinely available to local investigators. We carefully defined surgical procedure categories to identify patients undergoing major upper gastrointestinal surgery by either the abdominal or thoracic route. We also asked investigators to confirm whether the indication for surgery was cancer. The study also has a number of weaknesses. The ISOS project was prospectively

designed to allow us to clearly identify patients undergoing upper gastrointestinal surgery, but its' main objective was to evaluate all elective in-patient surgery. Baseline data were not specific to the upper gastrointestinal surgical procedure category, and our multivariable model may not fully account for high mortality rates in hospitals specialising in more complex surgery due to the low number of patients recruited in each centre. It is possible, that given the pragmatic nature of ISOS study looking at only complications during the hospital stay, we missed some of the later events, possibly resulting in an under-estimate of the incidence of postoperative complications. Also, due to the pragmatic nature of the study, external verification of the imputed data was not possible, potentially resulting in misreporting of complications. However, the similar studies from different countries also limited their data collection period to in-hospital stay or 30 days postoperatively and suffered from lack of external data verification.[16,25-28]

Conclusions

The findings of this international cohort study indicate that a large number of patients develop complications after elective in-patient upper gastrointestinal surgery. Patients undergoing major cancer surgery were at particular risk with complication rates approaching one in two patients. To improve patient outcomes, the concept of perioperative medicine is being adopted more widely to ensure safe and effective patient care throughout the perioperative care pathway.[39] International datasets help to set out the baseline for further quality improvement initiatives and can be used for perioperative decision-making and informed consent during upper gastrointestinal surgery.

Conflict of interest statement

RP has given lectures and/or performed consultancy work for Nestle Health Sciences, Medtronic, Edwards Lifesciences, GlaxoSmithkline and BBraun, and has received research funding from Nestle Health Sciences, BBraun, and Edwards Lifesciences, and is a member of the Associate editorial board of the British Journal of Anaesthesia. All other authors declare they have no conflicts of interest.

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Contributors

RP conceived the analysis and designed this with TS and JP. Patient recruitment and data collection were performed by the members of the International Surgical Outcomes Study group (see Appendix). TS and JP performed the data analysis. The manuscript was drafted by TS and RP, and then revised following critical review by all co-authors.

Data sharing

The authors are happy to consider data sharing requests from bona fide researchers. Participant consent was not obtained but the presented data are anonymised and risk of identification is low. Enquiries should be addressed to the chief investigator at: admin@isos.org.uk.

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